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Advisors Clear Herceptin; Find Tamoxifen Indicated For "Short Term Risk Reduction"

In two landmark actions, the FDA Oncologic Drugs Advisory Committee last week recommended approval for Herceptin as a treatment for metastatic breast cancer and expanded the label of Nolvadex for short-term reduction of risk of breast cancer in high risk populations.

By recommending approval for Herceptin (trastuzumab), sponsored by Genentech, the committee gave a green light to the first monoclonal antibody-based therapy for breast cancer. In the process of expanding the label for Nolvadex (tamoxifen citrate) to make it the first agent for reducing the risk of breast cancer, the committee had to assess the

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In Brief:

Karmanos Institute Names Four To Faculty; $1.5M Donated To Kaplan Cancer Center

KARMANOS CANCER INSTITUTE in Detroit appointed four new faculty members. **Joseph Fontana** was named director of Veteran's Administration Research Programs at Karmanos and chief of oncology at the Dingell VA Medical Center. He is also professor of oncology and internal medicine at Wayne State University. He was chief of hematology/oncology at the Baltimore VA Medical Center. **William Hryniuk** is director of technology assessment in the institute's Center for Cancer Economics, Technology Assessment, Innovation and Development. He will also serve as professor in the Division of Hematology and Oncology at WSU and interim director of the institute's clinical breast program. Hryniuk was director of the cancer center at the University of California, San Diego. **Andrew Sloan** was named assistant professor for the center and the Department of Neurological Surgery at WSU. He previously completed training at University of California, Los Angeles, and was a fellow in neurosurgical oncology and stereotactic neurosurgery at M.D. Anderson Cancer Center. **Michael Tainsky** was appointed program leader of cancer genetics at Karmanos and professor in molecular medicine and genetics, pathology, and biological sciences, at WSU. He was a professor in the Department of Tumor Biology at M.D. Anderson. . . . **DANIEL ROSES**, Whitehill professor and director of the Comprehensive Breast Cancer Center at the Kaplan Comprehensive Cancer Center of New York University, received a $1.5 million gift from the estate of Leo Shifrin. The gift will sponsor multidisciplinary pilot research projects and other

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ODAC Translates BCPT To Tamoxifen Package Insert

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significance of the Breast Cancer Prevention Trial.

In other actions taken during the three-day meeting, ODAC voted unanimously against recommending approval for Metaret (suramin hexasodium for injection), a treatment for metastatic prostate cancer sponsored by Parke-Davis, and voted to recommend approval for the following drugs:

—Camptosar (irinotecan hydrochloride) Injection for the treatment of metastatic colorectal cancer after failure 5-FU therapy. The drug, sponsored by Pharmacia & Upjohn, is the first treatment for metastatic colorectal cancer to be recommended for full approval in over 40 years. In 1996, the drug received an accelerated approval for metastatic cancer of the colon or rectum that has recurred or progressed after 5-FU therapy.

—Photofrin (porfimer sodium) for Injection for the reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial non-small cell lung cancer. The committee voted 8-0 to recommend approval for the SNDA from QLT PhotoTherapeutics Inc. of Vancouver. The drug is approved for palliative treatment for esophageal cancers and early-stage microinvasive lung cancer.

—Valstar (valrubicin) for patients with carcinoma in situ of the bladder refractory to bacillus Calmette-Guerin therapy and in whom cystectomy is medically contraindicated. The drug is sponsored by Anthra Pharmaceuticals Inc. of Princeton, NJ.

From Prevention Trial to Package Insert

Last April, the announcement that the Breast Cancer Prevention Trial demonstrated a 45 percent reduction in breast cancer incidence among women at high risk of developing the disease was met with much jubilation (**The Cancer Letter**, April 10).

Last week, ODAC was asked to guide FDA in translating the conclusions of the trial into the language of a package insert for tamoxifen. In a nutshell, the committee was asked to make a recommendation that required a re-examination of the definition of prevention and the definition of benefit in a prevention trial.

The stakes were high. Since tamoxifen for the prevention indication is expected to be prescribed by general practitioners and gynecologists, the recommendation by ODAC may have represented the final opportunity for oncologists to influence the manner in which the drug would be prescribed.

First, the committee eliminated the word "prevention."

"I have a concern with the use of the word prevention," said George Sledge, a consultant to the committee and professor of medicine and pathology at the Indiana Cancer Pavilion. "This is a trial with very short follow-up. Everything we know about breast cancer is that it's a disease that takes a long time to go from premalignant to invasive malignant state. And here we are seeing the effects within a year of starting the drug. While these may be beneficial effects, they are not prevention in the way that scientists understand the word `prevention.' I would be comfortable saying that it demonstrated `risk reduction.'

"This is a very well controlled trial," Sledge said. "I don't think it has met the bar where scientists would consider it a chemopreventive effect."

Out went the word "prevention," and the committee turned to defining the populations most likely to benefit from tamoxifen as a means of "risk reduction."

"I think the study demonstrated something like risk reduction or delay in diagnosis in a group of women at increased risk," said Richard Simon, chief of the NCI Biometric Research Branch. "I am not very sure what that group is. I don't think it has

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demonstrated it in women in general at an increased risk. I think there is a problem characterizing who they are."

Is it possible—or appropriate—to define this group?

It is not, said Norman Wolmark, chairman of the National Surgical Adjuvant Breast and Bowel Project, which led the trial.

"I think this is inherent problem in every clinical trial you do," Wolmark said. "You set out the eligibility criteria, and whoever actually enters the trial may or may not fulfill the entire spectrum of the eligibility criteria. But does that justify anyone from going back and retrospectively culling out a subset to say that this is more representative than those individuals who actually entered the trial? We don't have the power to do that. But, from my perspective, and more importantly, we don't have a right to do that."

Ultimately, the committee voted 11-0 that the prevention trial was an "adequate and well-controlled trial demonstrating short-term reduction of incidence of breast cancer in women entered in the trial."

With this determination out of the way, the committee moved on to the question of determining whether the prevention trial demonstrated that tamoxifen has a "favorable benefit/risk ratio" in prevention of breast cancer. After striking the offending word "prevention," the committee turned to the definition of "benefit" in a prevention trial.

"I have two concerns," said NCI biostatistician Simon. "One is, there is some uncertainty as to what the population that actually achieves short-term benefit is. The second concern is that I think this incorporates that [in determining] risk/benefit, you have to think in terms of long-term-effect. I think there is a great uncertainty in terms of what the long-term mortality benefits are, given that most of the tumors that are prevented or delayed are going to be curable by surgery plus tamoxifen.

"I think that when we talk about the risk ratio, there are many women who have satisfied the eligibility criteria for this trial—women who are 60 years old with no risk factors, for whom I believe the risk-benefit ratio is not favorable. The long-term benefits are relatively small. The risks are large. The risks apply to all the women, and the benefits apply to all.

"Since the reduction in breast cancer mortality is likely to be small, we need to be focusing on a quite high-risk population, or a population who are not so subject to the risks," Simon said.

"Richard, you are torturing us as only a statistician can," said Derek Raghavan, associate director of the University of Southern California Norris Comprehensive Cancer Center. "To be honest with you, this group of 13,000 courageous volunteers over time demonstrated that those people who were exposed to tamoxifen for five years or less had less breast cancer, which is a good thing... You could potentially [insert] a caveat that at the present time, those women most likely to benefit have not been identified, but we can't do more than that, because the data are just not there."

Since tamoxifen has been in use for decades, its safety profile is well known, Sledge said. "So the real question is, how do we define benefit? Do we define benefit in terms of short-term incidence? Do we define benefit in terms of a survival advantage? If we are going to set that bar, we would have to develop an entirely new set of studies and pretend for the next 20 years that we don't have the results of P-1 [the BCPT]."

SIMON: "We know something about the survival rates of node-negative, ER-positive breast cancer."

SLEDGE: "I will tell you that, having buried several women with ER-positive, node-negative breast cancer, I will not take quite as blasé view of it."

SIMON: "I am not saying it's 100 percent. I am saying that we know something about what it is."

SLEDGE: "We know that it's better than having lots of positive lymph nodes."

In a 9-2 vote, the committee found that the benefit-risk ratio of tamoxifen for short term reduction of risk of breast cancer is acceptable.

The committee recommended against recommending annual endometrial sampling and eye exams for women who take tamoxifen to reduce the risk of breast cancer. However, the committee said the company should be asked to conduct phase IV studies of trial participants who experienced thromboembolic events.

Ultimately, it will be up to patients and physicians to determine whether the side effects of tamoxifen are worth the risk, several committee members said.

"I think this drug should be approved, because doctors and patients should be allowed to decide this issue on the individual basis," Sledge said. "Having said that, I am tremendously concerned about how it

will be used. And for a chemoprevention drug, there probably should be a higher bar in terms of doctor-patient communication and specifically because of the onus on the company and on the NCI chemoprevention branch to provide information to patients.

"I would be quite happy making my recommendation dependent on real evidence that NCI and the company are going to put real resources into patient education and doctor education on that issue," Sledge said.

Minutes after Sledge spoke, a Zeneca press release announced that ODAC had recommended tamoxifen "for reduction of the incidence of breast cancer for in women at increased risk."

The words "short term" did not appear in the press release.

Herceptin: "The Data Are Quite Striking"

The committee voted unanimously, 11-0 to recommended approval of Herceptin as a single agent for second and third line treatment for metastatic breast cancer.

In discussion of Herceptin's role in first-line treatment regimens, the committee unanimously recommended approval of the agent in combination with Taxol.

"I think the data are quite striking, perhaps the greatest demonstration of clinical synergy that I've seen in solid tumor therapy," Richard Schilsky, director of the University of Chicago Cancer Center and chairman of the Cancer and Leukemia Group B, said at the ODAC meeting Sept. 2.

However, in a 9-2 vote, the committee decided that the risk of cardiotoxicity of the combination of Herceptin and an anthracycline therapy outweighed potential benefits.

"I think Herceptin produces synergistic cardiotoxicity with Adriamycyn, and I am not at all sure that the very modest though real clinical benefit of increased time to progression is really worth this synersistic cardiotoxicity," said James Doroshow, director of medical oncology and therapeutics research at City of Hope National Medical Center.

Questions presented to the panel included the following comparison of Herceptin and Taxol versus Taxol alone:

"When compared with paclitaxel alone, Herceptin used in combination with paclitaxel (175 mg/m^2) infused over three hours, was associated with a greater median time to progression by 4.2 months (2.5 months for paclitaxel versus 6.7 months for paclitaxel and Herceptin, p=0.001) and a higher one-year survival rate (61% for paclitaxel versus 73% for paclitaxel and Herceptin, p=0.1), but no significant difference in median survival. Herceptin in combination with paclitaxel was associated with infusional toxicity. In patients receiving TH, there was an observed 11% incidence of cardiotoxicity, as compared with 1% in patients treated with T alone. The incidence of class III or IV cardiotoxicity was 4% for patients treated with TH, compared with 1% for patients receiving T alone. Other toxicities which appeared to be increased when compared to patients receiving paclitaxel alone included anemia, leukopenia, abdominal pain, diarrhea, vomiting, and infections."

The FDA staff comparison of risks and benefits of anthracycline in combination with Herceptin versus AC therapy alone stated:

"When compared to AC (doxorubicin 60mg/m^2 or epirubicin 75 mg/m^2 plus cyclophosphamide 600 mg/m^2) chemotherapy, Herceptin used in combination with AC chemotherapy was associated with a greater median time to progression by 2.1 months (6 months AC vs, 8.1 months ACH, p,0.001) and a higher one-year survival rate (73% AC vs. 83% ACH, p=0.04) but no significant difference in median survival. Herceptin in combination with AC was associated with infusional toxicity. The observed incidence of cardiotoxicity in patients receiving ACH was 28%, as compared to an incidence of 7% in the AC arm).

The incidence of class III or IV cardiotoxicity was 19% in patients receiving ACH, compared with 2% in patients treated with AC alone. Other toxicities which appeared to be increased in incidence and severity when compared to patients receiving AC alone include: anemia, leukopenia, abdominal pain, diarrhea, dyspenia, and infections."

Herceptin is expected to be used for breast cancer patients who overexpress the HER2 protein.

Overexpression of HER2, which occurs in 25 to 30 percent of breast cancer patients, is associated with more aggressive disease and shortened survival in retrospective studies. Overexpression can be determined by a test performed on a new or stored specimen of tumor tissue.

Approval of that test was recommended Sept. 4 by a joint committee of the FDA Hematology and Pathology Devices Panel and Immunology Devices Panel. A positive test result will aid in the assessment

of patients for treatment with Herceptin. The assay, which is patented by Genentech, has been licensed by DAKO A/S of Copenhagen.

According to Genentech, Herceptin, in combination with chemotherapy in a randomized controlled trial involving 469 patients, was shown to produce a favorable clinical outcome, improving overall response rates from 28% in women treated with chemotherapy alone to 43% with Herceptin added, a 53% increase.

The median time to disease progression increased from 4.5 months in chemotherapy alone to 7.3 months in the Herceptin-plus-chemotherapy group. Median time to disease progression is measured from the time the patients are enrolled in the clinical trial until the time that an increase in tumor size or the appearance of a new tumor mass is assessed.

Of the 469 patients who entered the study, 78% of women treated with Herceptin-plus-chemotherapy were alive after one year, compared to 67% of women treated with chemotherapy alone, a relative increase of 16%.

A survival benefit has rarely been demonstrated in previous metastatic breast cancer studies. The data show no difference in median survival.

In a trial of 222 women, Herceptin used alone, 14% (31 out of 222) of women who had failed one or two prior chemotherapy regimens had objective tumor responses with tumor shrinkage of 50% or greater. Tumor response to Herceptin was also shown to be durable with a median duration of response of 9 months. Median survival in the single-arm study was 13 months, the company said.

In both trials, Herceptin was associated with mild infusion-associated symptoms in about 40 percent of patients, the company said.

In women taking Herceptin alone, hair loss and other commonly observed side effects associated with chemotherapy were not observed, the company said. Herceptin use was associated with diarrhea, low white blood cell count and infections.

In a related development, a coalition of five breast cancer organizations calling themselves the Herceptin NOW Oversight committee demanded in letters to FDA and Genentech officials that the drug be approved by Sept. 25.

The coalition includes the Breast Cancer Fund, the Cancer Support Community, Colorado Breast Cancer Treatment Committee, Marti Nelson Cancer Research Foundation, and SHARE.

In Congress:

Senate Committee Approves 15 Percent Increase For NCI

The Senate Appropriations Committee last week unanimously approved a fiscal 1999 appropriations bill for the Departments of Labor, Health and Human Services, and Education that includes $2.927 billion for the National Cancer Institute.

The amount would give NCI an increase of $384 million, or 15 percent, over the Institute's current appropriation, and $158.5 million more than President Clinton's request.

The bill, reported out of the committee on Sept. 3, provides a total of $15.6 billion for the National Institutes of Health, an increase of $2 billion over the FY98 appropriation.

The committee adopted an amendment proposed by Chairman Ted Stevens (R-AK) that directs NIH to spend $175 million on prostate cancer research.

Advocates for cancer research said they were pleased with the amount the Senate committee allocated to NCI and NIH. The House Appropriations Committee allocated $2.787 billion to NCI, a 9.1 percent increase (**The Cancer Letter**, July 17).

"The next benchmark is to get the House and Senate bills to the floor of each chamber," said Marguerite Donoghue, vice president for research and regulatory affairs of Capitol Associates Inc., a government relations firm based in Washington, DC. "Based upon our Hill sources, we understand there will be significant problems in moving the House bill to the floor. Some of those same issues could hamper the Senate consideration.

"The cancer community ought to be urging the members of the Senate to move this bill quickly," Donoghue said.

The House bill cuts $2 billion from education programs, and includes measures advocated by conservative Republicans that make the bill unacceptable to moderates on both sides of the aisle.

The Senate bill may have a greater chance of being passed, Capitol Hill sources said.

It is not likely that the bills will be approved and reconciled by a conference committee by Sept. 30, the last day of FY98, sources said. Congress would need to pass a continuing resolution to keep NIH and other agencies. Under this scenario, Congress would pass an "omnibus" funding bill early

next year. However, if neither HHS appropriations *bill is* approved, advocates for NIH say they will be in a weaker position to lobby for substantial increases to be included in an omnibus bill.

Senate Appropriations Committee Report

In the report of the Senate Appropriations Committee accompanying the Labor, HHS, Education bill, the committee urged NCI to increase research on the following cancers: breast, colon, hepatocellular, lymphoma, neurofibromatosis, ovarian, pancreatic, prostate, and urologic.

The committee also encouraged NCI to increase support for:

—Clinical trials and translational research

—Skeletal metastasis of myeloma, breast cancer, and prostate cancer.

—Primary immune deficiency diseases

—Nutrition in cancer prevention

—Imaging technologies, particularly digital mammography

—Cancer prevention and detection in native Hawaiians

—"Heat shock proteins"

—Behavioral science

Following are excerpts from the report:

The committee continues to regard scientific investigation into the cause, cure, prevention, and treatment of cancer as one of the nation's top priorities. Research offers the only hope for putting a stop to a disease that wastes precious human resources and contributes to spiraling health care costs. The committee was pleased to learn of recent studies documenting a reduction in death rates and improved rates of cancer morbidity and mortality as a result of smoking cessation....

Breast cancer—The committee continues to believe that an intensive research program on breast cancer should be among the top priorities of NCI and NIH.... The committee urges NCI to strengthen its funding commitment to breast cancer research. The committee urges NCI to expand research into the occupational causes of breast cancer, tumor biology, immunology, molecular medicine, and development of new treatment methods. Research is also needed to develop better prevention and detection strategies.

The committee notes that breast cancer incidence and mortality are higher than the national average in several states in the Northeast. The committee encourages the Institute to provide increased funding for regional breast cancer centers that would target areas of the country where the morbidity and mortality rates of breast cancer are higher than the national average.

The committee encourages the Institute to provide increased funding for a breast cancer research initiative designed to assist in minority cancer control, prevention, and treatment, particularly among Asian-American women.

Cancer coordination—The committee encourages NCI to continue its leadership role as coordinator of the national Cancer Program. As the facilitator of the nation's fight against cancer, the NCI specifically is encouraged to continue to work in collaboration with private/voluntary sector organizations, the CDC, and other federal agencies to address the coordination challenges outlined in the National Cancer Advisory Board's report entitled "Cancer at a Crossroads."

Cancer Information Service—The committee commends NCI for the creation of the toll-free Cancer Information Service; however, it is aware of a May 1998 report issued by the HHS Inspector General which concluded that nearly one-third of those who call the toll-free number have failed to reach a cancer information specialist. The committee notes that residences of Florida had the highest busy rate, with more than one-half the callers getting busy signals. The committee further notes the report concludes that resources were not equitably allocated among the 19 regions. The committee requests that the director of NCI issue a report to Congress not later than May 1, 1999, which provides specific initiatives to address the concerns raised in the report of the HHS Inspector General.

Clinical trials—The high cost of clinical trials and lack of third-party insurance coverage for any treatment considered experimental has made this critical bedside research arduous and difficult. The committee encourages NCI to place a greater emphasis on funding clinical trials, and to continue its efforts to establish mechanisms to ensure that the basic research conducted through NCI is translated to clinical benefit when appropriate.

Digital mammography—Digital mammography technology is currently undergoing testing for FDA approval.... However, large-scale testing of approximately 100,000 women is necessary to quantify its increased detection success relative to conventional film mammography. The committee believes NCI should provide Congress with a plan to manage such a large-scale trial in its fiscal year 2000 hearings....

Translational research—The committee has been made aware of the extraordinary explosion of scientific advances in cancer biology, immunology, and molecular biology and genetics that have occurred in recent years as a result of previous investments in basic research. These advances provide unprecedented opportunities to develop new therapies, early detection technologies, and prevention strategies. The committee is concerned that the translation of these promising discoveries into practice is not keeping pace with the opportunities that exist due to changes in the health care marketplace and weakness in the infrastructure for translational research. The

committee requests that NCI evaluate the barriers and impediments that inhibit clinical testing of new technologies such as vaccines, gene therapies, monoclonal antibodies, and be prepared to discuss the steps needed to remove these barriers at next year's appropriations hearing.

Pancreatic, prostate, and colon cancer—The committee supports increased efforts in the areas of pancreatic, prostatic, and colon cancer.... A portion of the amount provided should be devoted to research programs in these areas, particularly programs that utilize the newly discovered CaSm gene for gene therapy of pancreatic cancer; the newly implicated ETS2 gene for prostatic cancer; and the well-described DRA gene for colon cancer....

The committee continues to be very concerned about the high rates of incidence and mortality related to prostate cancer, particularly among African-American males.... The committee is encouraged by NCI's collaborations with the Department of Defense in combating this devastating disease and urges NCI to continue to strengthen and expand its prostate cancer research portfolio.

The committee encourages NCI to explore the feasibility of developing a national model research, education, training, and treatment center focusing on early diagnosis, prevention, and treatment of prostate cancer.

The committee also requests that the director of NIH, together with the director of NCI, submit a report to the Appropriations Committees, no later than April 1, 1999, outlining the activities NIH is undertaking to enhance prostate cancer research programs.

Smoking intervention study—Consistent with the budget request, the committee agrees that the American Stop Smoking Intervention Study be moved to CDC. The committee expects NCI to transfer the $25 million expended in fiscal year 1998 for ASSIST to CDC to continue this program. The committee continues to believe that NCI has a critical role to play in preventing and reducing tobacco use and its adverse health consequences. Tobacco use is responsible for at least one-third of all cancers and NCI resources should better reflect this. The committee believes that NCI must expand its existing tobacco-related research portfolio with a greater emphasis on behavioral, community, and state intervention research.

Outreach and public education—The committee commends NCI's dedication to the National 5-A-Day Campaign.... The committee encourages NCI to consider increasing its communications and communications research for the 5-A-Day program from its previous levels and increase its research in fruits and vegetables nutrition.

Gene therapy—The committee notes the outstanding progress being made by organizations studying the use of gene therapy in finding a cure for several forms of cancer. The committee is impressed by the progress being made by the Human Gene Therapy Research Institute at the Iowa Methodist Medical Center in Des Moines, IA, in finding a cure for breast cancer. The committee encourages the Institute to support organizations like this conducting breast cancer research utilizing autologous bone marrow transplantation and gene therapy methods.

Primary immune deficiency diseases— The committee urges NCI to establish a trans-institute initiative with NIAID, NICHD, and NHGRI by sponsoring a symposium of leading experts in cancer, immunodeficiencies, pediatrics, and genetics to explore the most promising areas of research and develop a comprehensive agenda for future research initiatives....

Nutrition and cancer—The committee continues to be extremely supportive of the Cancer Prevention Program, particularly the nutrition research component.... The committee hopes that the Cancer Prevention Program and nutrition research will have added significance in the new organizational structure recently implemented at NCI. The committee is particularly concerned that NCI utilize existing clinical nutrition research units and general clinical research centers to carry out investigation regarding the role of nutrition in cancer prevention....

Diethylstilbestrol—NCI and other Institutes, along with the Office of Women's Health, have developed a plan for expanded research activities in this area. The committee has included sufficient funds to carry out this plan.... The committee has included sufficient funds for NCI to contract with CDC to undertake educational efforts targeting consumers and health professionals on a national basis....

Complementary and alternative cancer therapies—The committee expects NCI to work collaboratively with the Office of Alternative Medicine to support expanded research on promising complementary and alternative cancer therapies, and on their integration with traditional therapies. Thousands of Americans are turning to these therapies and consumers will benefit from the results of rigorous scientific review. The committee expects to be briefed on the progress of the Institute's efforts prior to the next appropriations cycle.

Cancer in minorities—The committee remains concerned over recent statistics citing higher incidences of cancer among the native Hawaiian population.... The committee encourages continued research in the areas of prevention and detection, utilizing nurse practitioners in community-based centers for screening and education for the underserved populations.

Heat shock [proteins]—The committee is aware of a new technology that employs heat shock proteins to provide a genetic fingerprint of cells that allows for the identification of irregularities in cells. This technology could lead to the development of vaccines based on irregularities found in particular cells. The committee encourages NCI to support further investigation into this area.

NCI Programs:

Institute Seeks White Papers On Technology Development

The National Cancer Institute plans to provide $48 million over the next five years to support contracts for the development of new technologies in cancer research.

The new Unconventional Innovations Program would fund the development of technologies that would use the molecular profiles of cancer that are expected to be discovered through the Institute's Cancer Genome Anatomy project. Researchers plan to correlate these molecular profiles with characteristics of cancers, such as prognosis and response to therapy.

"Building upon molecular profiling, we wish to create technology platforms that will revolutionize cancer detection, diagnosis and treatment," according to a description of the program on the NCI website at http://amb.nci.nih.gov/uip.htm.

"NCI is interested in identifying technology systems or components that will enable sensing of molecular alterations in the body in a way that is highly sensitive and specific, yet non-intrusive," the statement said. "Molecular profile information would then be transmitted to external monitoring devices that would provide input to the physician."

The NCI Board of Scientific Advisors approved the program last June (**The Cancer Letter**, July 3).

To begin the new program, NCI is inviting scientists from academia, government, and industry to submit white papers on the development of "high-impact, long-range technologies that could fundamentally change the approach to the detection, diagnosis, and treatment of cancer," according to a Sept. 4 notice.

The white papers will help NCI develop a Broad Agency Announcement to be issued later this year or early next year. The BAA is a solicitation that describes an area of research and sets forth criteria for the selection of offers.

According to the notice, the goal of the new program is to develop technology platforms to enable the integration of:

—Non-invasive sensing of molecular alterations in vivo,

—Transmission of molecular information to an external monitor,

—Controlled intervention specific for the molecular profile,

—Monitoring of intervention.

White papers should address:

—Nature of the technological opportunity,

—Current capability of the technology,

—Technological barriers to meeting the defined goal,

—Contribution to the opportunity for the non-intrusive sensing, signaling, and intervention for cancer based on tumor specific molecular profiles,

—Potential impact on the detection, diagnosis, and treatment of cancer.

White papers should address areas of technology, not individual research projects. Proprietary information should not be included. Text should be limited to four pages or less. White papers should be clearly labeled with a cover sheet indicating "White Paper" and contact information for the author. Deadline for submission of white papers is Nov. 27, 1998.

White papers should be addressed to: Carol Dahl, Office of Technology and Industrial Relations, NCI, 31 Center Drive, Room 11A03, MSC 2590, Bethesda, MD 20892-2590. Phone 301-496-1550, fax: 301-496-7807. Email: carol_dahl@nih.gov.

In Brief:

CINJ Gets Grant From Novartis

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educational efforts in molecular biology and oncogenesis of breast cancer. . . . **CANCER INSTITUTE** of New Jersey has received a $500,000 grant from Novartis Pharmaceuticals to fund its program reducing barriers among minorities to participation in clinical trials at the institute. **William Hait** is director of the institute. . . . **DANIEL WEXLER**, formerly special assistant to the President and associate director of public liaison at the White House, has joined Capitol Associates Inc. as vice president of the Washington, DC, government relations firm. . . . **ROBERT HUEBNER**, 84, who studied viruses and cancer working as chief of the laboratory of infectious diseases at NIH in the 1960s and 1970s, died of pneumonia Aug. 26 at the VA Medical Center in Coatesville, PA. . . . **KARL FLORA**, director of the division of product quality research, FDA Center for Drug Evaluation and Research, died of non-Hodgkin's lymphoma Aug. 31 at Inova Fairfax Hospital in Fairfax, VA. He was 49. Before joining FDA in 1993, Flora worked for 16 years in NCI's Pharmaceutical Resources Branch.